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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/811,593	03/29/2004	Muhammad Anzar	MTC 2002.1 (37-21 (53264)	2857

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SENNIGER POWERS
ONE METROPOLITAN SQUARE
16TH FLOOR
ST LOUIS, MO 63102

EXAMINER	
GOUGH, TIFFANY MAUREEN	
ART UNIT	**PAPER NUMBER**
1657	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	02/08/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 02/08/2007.

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Office Action Summary	Application No.	Applicant(s)	
	10/811,593	ANZAR ET AL.	
	Examiner	Art Unit	
	Tiffany M. Gough	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/28/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed 11/28/2006 has been received and entered into the case. Claims 1-38 are pending and have been considered on the merits. All arguments and amendments have been considered.

Claim Objections

The claim objections over claims 18 and 19 have been withdrawn due to amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-17,19,20 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel et al (WO 02/043574, 6/6/2002 also published as PGPub US2004/0049801 A1) or Johnson (US 5,135,759) in view of D'Occhio (Animal Breeding, Use of New Technology, 1999).

Applicant claims a process for staining sperm cells comprising a staining mixture of sperm cells and a DNA fluorescent dye and further subjecting the mixture to temperatures in excess of 40°C. The mixture is subjected to the temperature for a sufficient amount of time to allow the dye to bind to the DNA. The desired period of time is from about 1-160 minutes and the dye concentration is from about 0.1-1000 μM. Applicant further claims adding a quencher to the staining mixture such as FD&C #40 and propidium iodide

Seidel et al disclose a method of staining sperm cells comprising a incubating sperm cells in a staining mixture comprising Hoechst 33342, i.e. a DNA fluorescent dye, at a concentration greater than 40 μM at temperatures between about 30°C and about 40°C for a time between 50-200 minutes, and further disclose optimizing these parameters by adjusting time, temperature and dye concentrations. (see claims, 0035,0036 and 0037).

Johnson discloses disclose a method of staining cells comprising staining sperm cells in a staining mixture comprising Hoechst 33342, i.e. a DNA fluorescent dye, at a concentrations ranging from 4-5μg/ml at temperatures between about 30°C and about 39°C for a time between 60-120 minutes, and further disclose optimizing these

parameters by adjusting time, temperature and dye concentrations(see column 4, lines 27-44).

Neither Seidel or Johnson teach the use of propidium iodide (PI) as a quencher in a staining mixture.

D'Occhio discloses a staining mixture comprising sperm in a semen buffer which is further incubated with Hoechst 33342 and propidium iodide (PI), i.e. a quencher, at temperatures of 32-35°C for 45-60 minutes (see p.252 first paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have added propidium iodide (PI) to a sperm staining mixture because D'Occhio teaches that PI quenches the fluorescence of Hoechst 33342, i.e. a DNA fluorescent dye, and only penetrates dead sperm (see p.252, first paragraph).

One of ordinary skill in the art would have been motivated to add a quencher such as PI because D'Occhio teaches PI as a quencher in a sperm staining mixture which is desirable because it quenches the fluorescence of Hoechst 33342 and only penetrates dead sperm which is beneficial during the sorting process (see p.252, first paragraph). One would reasonably have expected success in using PI as a quencher because it is known in the art as a quencher in staining mixtures comprising sperm and a DNA fluorescent dye.

Neither reference teaches incubating the staining mixture at temperatures exceeding 40°C for less than 30 minutes.

However, generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence

indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."). See MPEP 2144.05.

Claims 1-17,19-22 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel et al (WO 02/043574, 6/62002 also published as PGPub US2004/0049801 A1) or Johnson (US 5,135,759) in view of Guthrie et al (Molecular Reproduction and Development, vol 61, 2002)

Applicant claims a process for staining sperm cells comprising a staining mixture of sperm cells and a DNA fluorescent dye and further subjecting the mixture to temperatures in excess of 40°C. The mixture is subjected to the temperature for a sufficient amount of time to allow the dye to bind to the DNA. The desired period of time is from about 1-160 minutes and the dye concentration is from about 0.1-1000 μM.

Applicant further claims adding a quencher to the staining mixture such as FD&C #40 and propidium iodide.

Seidel et al disclose a method of staining sperm cells comprising staining sperm cells with a staining mixture comprising Hoechst 33342, i.e. a DNA fluorescent dye, at a concentration greater than 40 μM at temperatures between about 30°C and about 40°C for a time between 50-200 minutes, and further disclose optimizing these parameters by adjusting time, temperature and dye concentrations. (see 0035,0036 and 0037).

Johnson discloses disclose a method of staining sperm cells comprising staining sperm cells with a staining mixture comprising Hoechst 33342, i.e. a DNA fluorescent dye, at a concentrations ranging from 4-5μg/ml at temperatures between about 30°C and about 39°C for a time between 60-120 minutes, and further disclose optimizing these parameters by adjusting time, temperature and dye concentrations (see column 4, lines 27-44).

Niether Seidel or Johnson teach the use of a quencher in combination with their staining mixture, specifically FD&C#40 in combination with the dye Hoechst 33342.

Guthrie et al teach a staining mixture comprising a buffered sperm mixture, sperm in BTS, which is further treated with Hoechst 33342 and FD&C 40. FD&C#40 is added to quench the fluorescence of Hoechst 33342 in dead sperm to differentiate them from the living sperm in the sample (see p.88 Material and Methods section).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have added FD&C#40 to a sperm staining mixture because

Gunthrie teaches FD&C#40 to quench the fluorescence of Hoechst 33342, i.e. a DNA fluorescent dye, and to differentiate between living and dead sperm cells.

One of ordinary skill in the art would have been motivated to add a quencher such as FD&C#40l because Gunthrie teaches FD&C#40 as a quencher in a sperm staining mixture which is desirable because it quenches the fluorescence of Hoechst 33342 and only penetrates dead sperm which is known in the art to beneficial during the sorting process. One would reasonably have expected success in using FD&C#40 as a quencher because it is known in the art as a quencher in staining mixtures comprising sperm and a DNA fluorescent dye.

Claims 1-20 and 23 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel et al (WO 02/043574, 6/62002 also published as PGPub US2004/0049801 A1) or Johnson (US 5,135,759) in view of Garner et al (Biology of Reproduction, vol 53, 1995)

Applicant claims a process for staining sperm cells comprising a staining mixture of sperm cells and a DNA fluorescent dye and further subjecting the mixture to temperatures in excess of 40°C. The mixture is subjected to the temperature for a sufficient amount of time to allow the dye to bind to the DNA. The desired period of time is from about 1-160 minutes and the dye concentration is from about 0.1-1000 μM. Applicant further claims adding a quencher to the staining mixture such as FD&C #40 and propidium iodide.

Seidel et al disclose a method of staining sperm cells comprising staining sperm cells with a staining mixture comprising Hoechst 33342, i.e. a DNA fluorescent dye, at a concentration greater than 40 μM at temperatures between about 30°C and about 40°C for a time between 50-200 minutes, and further disclose optimizing these parameters by adjusting time, temperature and dye concentrations. (see 0035,0036 and 0037).

Johnson discloses disclose a method of staining sperm cells comprising staining sperm cells with a staining mixture comprising Hoechst 33342, i.e. a DNA fluorescent dye, at a concentrations ranging from 4-5μg/ml at temperatures between about 30°C and about 39°C for a time between 60-120 minutes, and further disclose optimizing these parameters by adjusting time, temperature and dye concentrations (see column 4, lines 27-44).

Niether Seidel or Johnson teach the use of a quencher in combination with their staining mixture, specifically propidium iodide in combination with the dye SYBR-14.

Garner et al teach the staining of sperm cells with SYBR-14 and propidium iodide, which is useful in determining the proportions of living and dead sperm cells in sperm samples (see introduction first paragraph). They teach the preparation of a dye buffered solution which is then added to a buffered sperm solution to stain the sperm cells (see Material and Methods section, specifically paragraphs 6-9).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have added propidium iodide to a sperm staining mixture because Garner teaches that as sperm die, they lose their ability to resist the influx of PI, which upon entering the sperm it quenches the SYBR-14 staining. They also note

that a similar effect was also seen when used in combination with with Hoechst 33342 (see Discussion section).

One of ordinary skill in the art would have been motivated to add a quencher such as propidium iodide because Garner teaches PI as a quencher in a sperm staining mixture which is desirable because it quenches the fluorescence of SYBR-14 and Hoechst 33342. One would reasonably have expected success in using PI as a quencher because it is known in the art as a quencher in staining mixtures comprising sperm and a DNA fluorescent dye.

Claims 1-15,24-28 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel et al (WO 02/043574, 6/62002 also published as PGPub US2004/0049801 A1) or Johnson (US 5,135,759) in view of Van Demark et al (US 3,005,756,1961) or Salisbury et al (Journal of Reprod. Fertility vol. 6, 1953).

Applicant claims a process for staining sperm cells comprising a staining mixture of sperm cells and a DNA fluorescent dye and further subjecting the mixture to temperatures in excess of 40°C. The mixture is subjected to the temperature for a sufficient amount of time to allow the dye to bind to the DNA. The desired period of time is from about 1-160 minutes and the dye concentration is from about 0.1-1000 μM. Applicant further claims a staining mixture comprising a carbonate buffer comprising 0.097 moles/L of $NaHCO_3$, 0.173 moles/L of $KHCO_3$ and 0.090 moles/L of $C_6H_8O_7 \cdot H_2O$ in water, which inhibits sperm motility.

Seidel et al disclose a method of staining sperm cells comprising staining sperm cells with a staining mixture comprising Hoechst 33342, i.e. a DNA fluorescent dye, at a concentration greater than 40 μM at temperatures between about 30°C and about 40°C for a time between 50-200 minutes, and further disclose optimizing these parameters by adjusting time, temperature and dye concentrations. (see 0035,0036 and 0037).

Johnson discloses disclose a method of staining sperm cells comprising staining sperm cells with a staining mixture comprising Hoechst 33342, i.e. a DNA fluorescent dye, at a concentrations ranging from 4-5μg/ml at temperatures between about 30°C and about 39°C for a time between 60-120 minutes, and further disclose optimizing these parameters by adjusting time, temperature and dye concentrations (see column 4, lines 27-44).

None of the references teach the composition to further comprise 0.097 moles/L of $NaHCO_3$, 0.173 moles/L of $KHCO_3$ and 0.090 moles/L of $C_6H_8O_7 \cdot H_2O$ in water.

However, Van Demark et al (US 3,005,756,1961) disclose the use of an inhibitory diluent containing $NaHCO_3$,$KHCO_3$ and $C_6H_8O_7 \cdot H_2O$ in water (see col. 5, lines 55-75).

Salisbury et al (Journal of Reprod. Fertility vol. 6, 1953) teach the use of a buffer which inhibits sperm motility. The buffers contain $NaHCO_3$,$KHCO_3$ and $C_6H_8O_7 \cdot H_2O$ in water (see p.352 Materials and Methods section), which are useful in determining which substrates are useful in the metabolism of spermatozoa (see p.352 1st full paragraph).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention was made to use such a motility inhibitory buffer claimed by Van Demark or Salisbury, in combination with the staining mixture because such buffer is discloses as being useful in examining the which substrates are beneficial for spermatozoal metabolism and economy.

One of ordinary skill in the art would have been motivated to add such carbonate buffers to a sperm containing composition because as stated above, they are beneficial for examining useful substrates. One would reasonably have expected success in inhibiting sperm motility using such buffers because both Van Demark and Salibury teach these components to have an inhibitory effect.

Neither Van Demark nor Salisbury teach the exact amounts of each components as those claimed by applicant.

However, it would be obvious to one of ordinary skill in the art at the time of the invention to adjust the buffer components to a concentration optimal for such invention, therefore optimizing these result effective variables is the result of routine experimentation.

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence

indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference

process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."). See MPEP 2144.05

Claims 1-15,29-34 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel et al (WO 02/043574, 6/62002 also published as PGPub US2004/0049801 A1) or Johnson (US 5,135,759) in view of Sabuer et al (Journal of Reproduction and Fertility, vol 20, 2000) or De Pauw et al (Biology of Reproduction vol 67, 2002) in further view of Bruemmer et al (Journal of Animal Science, vol 80, 2002).

Applicant claims á process for staining sperm cells comprising a staining mixture of sperm cells and a DNA fluorescent dye and further subjecting the mixture to temperatures in excess of 40°C. The mixture is subjected to the temperature for a

sufficient amount of time to allow the dye to bind to the DNA. The desired period of time is from about 1-160 minutes and the dye concentration is from about 0.1-1000 μM. Applicant further claims the process to include a composition comprising a composition which regulates oxidation/reduction reactions such as pyruvate in amounts ranging from about 0.5μM to 50mM.

Seidel et al disclose a method of staining sperm cells comprising staining sperm cells with a staining mixture comprising Hoechst 33342, i.e. a DNA fluorescent dye, at a concentration greater than 40 μM at temperatures between about 30°C and about 40°C for a time between 50-200 minutes, and further disclose optimizing these parameters by adjusting time, temperature and dye concentrations. (see 0035,0036 and 0037).

Johnson discloses disclose a method of staining sperm cells comprising staining sperm cells with a staining mixture comprising Hoechst 33342, i.e. a DNA fluorescent dye, at a concentrations ranging from 4-5μg/ml at temperatures between about 30°C and about 39°C for a time between 60-120 minutes, and further disclose optimizing these parameters by adjusting time, temperature and dye concentrations (see column 4, lines 27-44).

Neither Seidel or Johnson teach the staining mixture to contain a composition which regulates oxidation/reduction reactions such as pyruvate.

However, Sabeur teach a composition comprising spermatozoa in TALP buffer , i.e. pyruvate, and Hoechst 33258, i.e. a DNA selective dye (see p.136, material and methods section). TALP media is known in the art to contain pyruvate at amounts greater than 50μM. For support, see IVF protocols at

http://www.specialtymedia.com/05Resources/Protovols/ivfprotocol.htm. It is disclosed that TALP contains pyruvate in amounts of 0.5,1 and 2 ml, thus greater than 50μM.

De Pauw teach a composition comprising spermatozoa in TALP buffer, i.e pyruvate and SYBR-14, i.e. a DNA selective dye (see Materials and Methods section and p.10762nd full paragraph). TALP media is known in the art to contain pyruvate at amounts greater than 50μM. For support, see IVF protocols at http://www.specialtymedia.com/05Resources/Protovols/ivfprotocol.htm. It is disclosed that TALP contains pyruvate in amounts of 0.5,1 and 2 ml, thus greater than 50μM.

None of the references teach the composition to contain pyruvate at concentrations selected from 2.5,10,15,25 or 50 mM.

However, Bruemmer teaches the addition of pyruvate to sperm compositions in the amount of up to 10mM, but more preferable is the addition of between 2 to 5 mM of pyruvate. They teach that the addition of pyruvate to sperm compositions is beneficial because it maintains spermatozoal motion, it acts as an energy substrate and further (at high concentrations) acts as an antioxidant for spermatozoa (see p. 17,1st,2nd and 4th paragraphs).

It would have been obvious to one of ordinary skill in the art at the time of the invention was made to add pyruvate, at the claimed concentrations, to a sperm composition because Bruemmer teaches the addition of pyruvate, in amounts of 2 to 10 mM, to a sperm composition to be beneficial because it maintains spermatozoal motion, acts as an energy substrate and further (at high concentrations) acts as an antioxidant for spermatozoa (see p. 17,1st,2nd and 4th paragraphs).

Therefore, one of ordinary skill in the art would have been motivated to make such a modification to a sperm containing composition because such concentrations are disclosed as being beneficial to sperm and therefore, one would reasonably have expected success in making a sperm composition comprising the claimed amounts of pyruvate as suggested by Bruemmer.

It would be obvious to one of ordinary skill in the art at the time of the invention to adjust the buffer components to a concentration optimal for such invention, therefore optimizing these result effective variables is the result of routine experimentation.

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference

process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."). See MPEP 2144.05.

Claims 1,29,30,31,35-38 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel et al (WO 02/043574, 6/62002 also published as PGPub US2004/0049801 A1) or Johnson (US 5,135,759) in view of Remington (WO 02/077011 also US7015310 B2).

Applicant claims a process for staining sperm cells comprising a staining mixture of sperm cells and a DNA fluorescent dye and further subjecting the mixture to temperatures in excess of 40°C. The mixture further comprisies a composition which regulates oxidation/reduction reactions intracellularly or extracelllularly. The composition is selected from the group consisting of vitamin K and lipoic acid in amounts ranging from 1-100μM to 0.1-1.0mM respectively.

Seidel et al disclose a method of staining sperm cells comprising staining sperm cells with a staining mixture comprising Hoechst 33342, i.e. a DNA fluorescent dye, at a concentration greater than 40 μM at temperatures between about 30°C and about 40°C for a time between 50-200 minutes, and further disclose optimizing these parameters by adjusting time, temperature and dye concentrations. (see 0035,0036 and 0037).

Johnson discloses disclose a method of staining sperm cells comprising staining sperm cells with a staining mixture comprising Hoechst 33342, i.e. a DNA fluorescent dye, at a concentrations ranging from 4-5μg/ml at temperatures between about 30°C and about 39°C for a time between 60-120 minutes, and further disclose optimizing these parameters by adjusting time, temperature and dye concentrations (see column 4, lines 27-44).

Neither Seidel or Johnson teach the staining mixture to contain a composition which regulates oxidation/reduction reactions such as Vitamin K and lipoic acid.

However, Remington discloses the use of Vitamin K and lipoamide, i.e, lipoic acid, to study redox reactions intracellularly (see col. 15,16).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have added vitamin K and/or lipoic acid to a composition as oxidation/reduction agents because they are known oxidation/reduction agents because of their ability to donate and accept electrons.

One of ordinary skill in the art would have been motivated to add a redox agent such as Vitamin K or lipoic acid because Remington teaches both as redox agents used intracellularly . One would reasonably have expected success in Vitamin K or lipoic acid because they are disclosed in the art as acceptable redox agents.

Although the concentrations and temperatures claimed by applicant are not disclosed in the art, it would have been obvious to one of ordinary skill in the art at the time of the invention to adjust the process and buffer components to a concentrations and temperatures optimal for such invention, therefore optimizing these result effective variables is the result of routine experimentation.

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ

233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference

process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."). See MPEP 2144.05.

Thus ,the claimed invention as a whole is prima facie obvious over the prior art.

Response to Arguments

Applicant arguments have been considered, but are not found persuasive for the following reasons. Applicant argues that the primary references, Siedel and/or Johnson do not teach temperatures in excess of 40C. While this is true, they do suggest staining sperm cells with a DNA selective dye at temperatures up to 40C, with adjustments in time and temperature to preserve viability. Thus, given what is taught in the art of optimization to ensure sperm viability and in absence of evidence to the contrary, one of ordinary skill in the art would be motivated to optimize such parameters as routine scientific experimentation. One of skill in the art would be motivated to stain sperm at 40°C or more for shorter periods of time to test viability within the staining process. Applicant points to their figures for support in the claimed process, however figures 7-18 fail to be persuasive and lack clarity in supporting applicants unexpected results.

Applicant states that the Seidel reference does not indicate the temperatures at which frozen-thawed samples were stained. Applicants attention is directed to p.3, sol. 0035-0037, which state temperature between 30-40°C, and specifically 39°C for about 60 minutes.

Applicant argues the Johnson reference by reviewing and sighting the prosecution history of such case. However, the prosecution history is/was not relied upon for the rejection, only the teachings of Johnson, thus, applicants arguments are not pertinent to the instant case and claims under examination. Applicant arguments are not persuasive.

Applicant also argues that the Office has used applicants specification to establish a hindsight obviousness rejection. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). The rejections of record were made over the prior art of record, not including applicant specification.

Applicant arguments with respect to the 103 rejections made over Seidel or Johnson in view of D'Occhio, Guthrie, Garner, Saubeur, DePauw, Bruemmer et al, and Remington et al have been considered but are not persuasive. Applicant argues again

that neither Seidel or Johnson teach the claimed temperatures and lack of obviousness with respect to the primary references which are not remedied by the secondary references. The secondary references have been applied to show obviousness and motivation to use the claimed dyes, quenchers, and an oxidation/reduction composition in a process for staining sperm cells. As stated above with respect to the claimed temperature, given what is taught in the art of optimization to ensure sperm viability and in absence of evidence to the contrary, one of ordinary skill in the art would be motivated to optimize such parameters as routine scientific experimentation. One of skill in the art would be motivated to stain sperm at 40°C or more for shorter periods of time to test viability within the staining process. Applicant points to their figures for support in the claimed process, however figures 7-18 fail to be persuasive and lack clarity in supporting applicants unexpected results.

Applicant states that the Seidel reference does not indicate the temperatures at which frozen-thawed samples were stained. Applicants attention is directed to p.3, sol. 0035-0037, which state temperature between 30-40°C, and specifically 39°C for about 60 minutes.

Applicant arguments with respect to the 103 rejections made over Seidel or Johnson in view of Van Demark or Salisbury et al over claims 1-15, 24-28 have been considered but are not found persuasive. As stated above optimizing the temperature and time of staining is well within the purview of one of ordinary skill in the art. Thus, the temperature is obviated by the Johnson or Seidel references. Further, as stated above and in the previous office action. Both Van Demark and Salisbury teach a sperm

inhibitory diluent as claimed by applicant. Applicant argues the references teach the buffers as storage buffers however, Salisbury clearly teaches the composition as an inhibitory diluent rendering sperm cells immobile. The composition is known in the art as an inhibitory diluent for sperm cells, whether it is used in a staining process or as a storage buffer is intended use. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. Thus, the compositions taught in the art as inhibitory diluents do not create a structural difference and one of ordinary skill in the art would be motivated by the disclosure of its motility inhibiting properties to use it in a process for staining sperm cells as a motility inhibiting diluent.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tiffany M. Gough whose telephone number is 571-272-0697. The examiner can normally be reached on M-F 8-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Tiffany Gough

RUTH DAVIS
PRIMARY EXAMINER